Digitized by the Internet Archive
in 2018 with funding from
University of Toronto

https://archive.org/details/medjournalDec1947uoft

Volume XXV Toronto, December, 1947 Number 3

The University of Toronto Medical Journal

(AN UNDERGRADUATE PUBLICATION)

This journal is published six times a year, November to April, by the Medical Society of the University of Toronto, to serve as a medium for student expression and to bring to the student recent articles of scientific interest.

$1.50 per volume. 25c. per single copy.

ADVISORY STAFF

PROF. A. E. LINELL, M.D., Ch.B.(Manc)
J. H. COUCH, M.A., M.B., F.R.C.S.(Edin.), F.R.C.S.(C.)
J. HEPBURN, M.B., F.R.C.P.(C.)
D. Y. SOLANDT, M.A., M.D., Ph.D.(Lond.)
A. M. WYNNE, M.A. Qu., Ph.D.
H. H. HYLAND, M.D., M.R.C.P.(Lond.), F.R.C.P.(C)

Editor-in-Chief
E. A. McCULLOCH

Associate Editor
R. H. SHEPPARD

Assistant Editors
M. L. BUNKER
W. G. B. CASSELMANN

Managing Editor
F. L. CLEMENT

Features Editor
R. K. GRAHAM

Assistant Managing Editor
B. BERMAN

Abstracts Editor
E. R. YENDT

Circulation Manager
R. H. JOHNSON

Contributing Editors
R. W. RUTHERFORD
EDWARD FISH
B. E. PIVNICK
D. J. McCULLOCK
M. J. T. SEDLMEIR
S. A. WAX
MISS I. SHUBICK

Address all communications to Room 107, Anatomy Building

EDITORIAL

THE CURRICULUM COMMITTEE

In the final issue of the previous volume of this issue there appeared a report on better Staff-Student relations. An important recommendation has now been put into effect. The Curriculum Committee has been set up. Miss Dorothy Ley, the Chairman of Camsi, is the chairman of the committee, and Mr. M. L. Bunker and Mr. E. A. McCulloch are the members. The committee holds monthly meetings to consider suggestions for the improvement of the curriculum submitted to it by the students. It also discusses any matter affecting medical education. Both the agenda and the minutes of the meetings are submitted to the Dean for his consideration. Dr. Macfarlane has approved of this committee and has expressed his willingness to consider suggestions brought to him through it. We urge you to take advantage of this means of helping those who will follow you in the course by passing along the results of your experience.

CALMETTE'S VACCINE—B.C.G.

R. M. PRICE, M.B.

(*Department of Pathology and Bacteriology, University of Toronto*)

The bacillus of Calmette et Guerin is an attenuated bovine tubercle bacillus. The bacillus was isolated in 1909 from the milk of a tuberculous cow, and was for 250 generations, over a period of 13 years, grown on beef-bile-potato-glycerol medium. The strain which evolved is no longer capable of producing progressive tuberculosis. The nature of the change resulting in the loss of virulence is completely unknown. The loss of virulence appears permanent, and does not reappear on transfer to ordinary media.

Twenty-five years ago Calmette began to use his vaccine by feeding it to newborn infants. Since then the vaccine has been tried in most European countries, with the exception of the British Isles, and in North and South America. Over three million individuals have been voluntarily vaccinated without untoward results. No less than one million individuals have been vaccinated in the Scandinavian countries out of a total population of 13 million. In Canada the vaccine has been in use since 1926, chiefly in the Province of Quebec.

The advocates of Calmette's vaccine believe that this attenuated bacillus should be given to all tuberculin negative individuals. The successful localization of B.C.G. in the tissues of the host initiates a benign, self-limiting lesion; sensitises the host to tuberculin, and rather rapidly produces a variable degree of resistance to reinfection with virulent human or bovine tubercle bacilli.

The opponents to B.C.G. vaccination emphasize the dangers from such deliberate imposition of infection, no matter how benign, and insist that persons thus infected can develop tuberculosis, and furthermore, that this induced infection does not give significant immunity.

Preparation of the Vaccine

The vaccine is a suspension of living B.C.G. in a suitable diluent. The original Calmette strain is used everywhere. The vaccine is prepared from the bacillary membrane on the surface of fluid medium (Sauton's), grown for two weeks, freed from the medium by filtration, weighed, placed with a small amount of diluent in sterile flasks containing stainless steel beads, and shaken to make the bacillary emulsion as homogeneous as possible. The vaccine is put up in sterile ampoules containing 1 mg., 10 mgs., and 75 mgs. per cc. The vaccine is kept at refrigerator temperature. No vaccine more than eight days old is ever employed. Before use, the ampoules are vigorously shaken, to break up clumps, and to insure a uniform bacillary emulsion.

Methods of administering B.C.G.

1. Oral method. Used by Calmette and his associates. Three doses of B.C.G., 10 mgs. each, fed to infants in the first ten days of life.

2. Scratch method. Three to six linear scratches made on the upper arm, or back, and a drop of special emulsion (75 mgs. per cc.) of B.C.G. applied, and allowed to dry.

3. Multiple puncture method. A drop of the special B.C.G. emulsion referred to, is placed on the upper part of the arm, and thirty-five to fifty punctures made over an area of skin measuring 1 × 1.5 cms., piercing only the superficial layer of skin.

4. Intradermal method. 0.1 mg. B.C.G. each given intradermally in two areas in the deltoid region. The injection is given as superficially as possible, and injected as slowly as possible to avoid traumatizing the local tissues. Too deep an injection, too rapid an injection or trauma may lead to severe local reactions. The intradermal method of vaccination is the method of choice of workers in the United States, Canada and the Scandinavian countries.

Normally, if the vaccine "takes", a small nodule appears at the site two or three weeks after vaccination, which gradually fades away, leaving a reddish scar. However, in about 20% of individuals vaccinated by this method, the nodule increases in size, perforates the skin, and discharges a few drops of pus, in which a few of the bacteria can be demonstrated, or it may result in the formation of a shallow ulcer. The resultant ulceration may persist for six to eight weeks, when it completely heals, leaving a small tissue paper scar. There is no systemic reaction, and no associated glandular enlargement.

The advantage of this method over the others described is due to the fact that about 99% of individuals thus vaccinated become allergic to tuberculin, and the resultant immunity conferred upon them appears of longer duration than that conferred by any of the other methods described. With this method, allergy develops as early as 14 days after vaccination, and as a general rule, in 6 to 8 weeks.

Prior to vaccination, it is absolutely imperative to rule out allergy to tuberculin. This is done by the Mantoux test, giving an initial dose of 0.05 mg. of Old Tuberculin, and if negative, repeating the test with one milligram. Individuals weakly allergic, or those in the pre-allergic state, are very prone to give severe reactions to the vaccine. Hence the absolute necessity for ruling out allergy prior to vaccination.

Vaccination is contraindicated in individuals recently exposed to tuberculosis. It is advisable to wait at least six weeks after known exposure. It is advisable to remove vaccinated individuals from exposure to infection for at least six weeks, to enable their tissues to develop an adequate resistance to reinfection.

It is interesting that a single vaccination is sufficient to protect an adult, but on the other hand, children should be revaccinated annually for at least three or four years, in order to insure resistance to reinfection.

As already mentioned, over three million individuals have been voluntarily vaccinated with B.C.G. The disadvantage of such a mass experiment is of necessity, the lack of proper follow-up. Therefore the following controlled experiments are of interest and importance:—

Aronson and Palmer (1) in the United States in a study begun in 1935, vaccinated 1,550 tuberculin negative North American Indians, varying in age from 1 to 20 years. During this same period, 1,557 individuals served as controls. This group was followed for a period of six years with annual tuberculin tests and chest X-ray examinations. During this time, 28 deaths from tuberculosis occurred in the control group, as against 4 deaths in the vaccinated group. The total number of cases of tuberculosis, including deaths, was 185 in the control group, as against only 40 cases of tuberculosis, including deaths, in the vaccinated group. The authors therefore conclude that vaccination with B.C.G. is associated with definite protection against the development of tuberculosis, as measured by mortality and morbidity experience in the two groups included in their study.

Ferguson (2) in 1946 published the results of a study begun in 1934 and lasting through 1943. In all, 2,042 nurses in training in eight different hospitals in Saskatchewan were accepted for study. The average age in this group was 20 years. During this period, of the 1,005 nurses vaccinated with B.C.G., 9 developed manifest tuberculosis, or 0.895 per cent. Of the 759 negative non-vaccinated nurses, 29 developed manifest tuberculosis, or 3.82 per cent. Of the 278 positive reactors in this group, 3 developed manifest tuberculosis, or 1.08 per cent. The ratio of vaccinated negatives against non-vaccinated negatives is as 1:4.27.

There were no deaths in this older age group. Furthermore, when manifest tuberculosis developed in the vaccinated group, the lesions were less extensive than in the non-vaccinated negatives. The infecting strain was always the human type of B. tuberculosis.

Heimbeck (3) in Oslo began to vaccinate probationer nurses in 1927. Of 1,453 nurses studied, the morbidity from tuberculosis as per 1,000 was, 12.4 for tuberculin positive nurses; 141.2 for tuberculin negative nurses, and 24.1 for tuberculin negative nurses vaccinated with B.C.G.

Wallgren (4) in Stockholm states that B.C.G. is used extensively in vaccinating infants, and that the mortality from tuberculous meningitis in that age group is rapidly falling. (A recognized barometer of the amount of the disease in the community.) He further states that he has not seen a case of tuberculous meningitis develop in a vaccinated infant.

Holm (5) in Copenhagen, where prophylactic vaccination against tuberculosis with B.C.G. has been in effect since 1927, notes that the morbidity from tuberculosis in the adolescent and young adult group has been reduced to one-fourth.

Thus, statistical and clinical observations in the Scandinavian countries, and controlled experiments in the United States and Canada with B.C.G. show that both the morbidity and mortality from tuberculosis has been reduced in the vaccinated groups. The fact that over one million individuals have been voluntarily vaccinated in the Scandinavian countries alone, indicates clearly that there could not have been any serious complications.

Summary and Conclusions:

1. B.C.G. is an attenuated bovine tubercle bacillus.
2. The successful localization of B.C.G. results in the production of a benign, self-limiting lesion; the sensitization to tuberculin, and a marked degree of resistance to reinfection with virulent human or bovine tubercle bacilli.
3. In infants and young children the duration of immunity conferred is rather short, therefore re-vaccination is indicated.
4. A single vaccination appears sufficient to protect an adult.
5. Only 0.5 to 1 per cent of individuals fail to develop allergy as a result of vaccination.
6. The immunity conferred with B.C.G. is relative, and not absolute.
7. The concensus is that Calmette's vaccine is harmless, and can not produce active tuberculosis.

REFERENCES

Aronson, J. D. and Palmer, C.E.: U.S. Public Health Reports, June 1946, 802.
Ferguson, R. G.: Can. Jour. Public Health, 1946, 37, 435.
Heimbeck, J. et. al.: Lancet, 1947, 2, 438.

ACUTE ANTERIOR POLIOMYELITIS

JOHN PALMER 4T8

Poliomyelitis is an acute, infectious disease caused by a filterable virus, often resulting in a flaccid paralysis.

It should be noted that the term "infantile paralysis" is a misnomer. In the past few years, the trend of age incidence has been upwards, and now, young adolescents are most frequently stricken. No age group is exempt.

The virus of poliomyelitis is one of the smallest of the viruses (10-15 μ). It has been demonstrated that there are many different strains, varying in virulence, which may explain the variations in the severity of outbreaks, the failure of convalescent serum and the occasional occurrence of second attacks.

I. Epidemiology

The Disease is Communicable

It is known that active cases are able to transmit the disease to others who may not develop paralysis. Laboratory investigations have demonstrated the presence of the virus in healthy contacts. The occurrence of many serious epidemics proves that it is a communicable disease.

Source of Infection

The source of the infection is man. The virus has been found in the nose and throat secretions of acutely ill patients and in the stools of acute and convalescent cases.

Transmission

Spread by contact is a likely method because of the ease of transmission of nose and throat secretions. However, the occurrence in epidemic form during the summer suggests an insect vector and experiments have shown that flies may spread the virus by fecal contamination of food. It has recently been shown that certain strains of the virus are highly infectious by the intracutaneous route. Water from sewage contaminated rivers and swimming pools may be a vehicle in the spread of infection. It is known that the virus of poliomyelitis can exist in water for a month.

Precautions to Prevent Spread

When a case has occurred in a household, the patient should be isolated and contacts quarantined. A high standard of personal hygiene is important. Adequate steps should be taken to disinfect excreta before disposal and to prevent the spread of the infection to food or drink by contaminated hands or flies.

II. Pathology

The lesions are widely distributed throughout the central nervous system, being most marked in the anterior horn cells, but also affecting the posterior horn

cells and white matter, medulla, pons, midbrain, dentate nucleus, and to a lesser extent the motor area of the brain.

1. Stage of Inflammation

The cord is edematous and hyperemic—the meninges congested. Inflammatory cells are present as perivascular infiltrations and as focal areas of inflammation which may show necrosis.

2. Stage of Degeneration

This is more marked in the spinal cord than in the brain. The anterior horn cells are chiefly affected. The degeneration may vary from chromatolysis to complete disappearance of the cell.

III. Clinical Picture

There are three common types:

1. Abortive Poliomyelitis
2. Paralysis of Spinal Origin
3. Bulbar Paralysis.

The course of the disease is as follows:

Stage I

(1) Temperature varies from 100-102°F.—seldom higher
(2) Headache—usually frontal
(3) Tiredness and drowsiness
(4) Soreness and aching in various muscles
(5) Gastro-intestinal disturbance
—nausea, commonly vomiting
—anorexia
—constipation—diarrhoea is uncommon
(6) Respiratory infection
—complains of mild head cold
—nasopharynx commonly shows congestion.

These symptoms are usually interpreted as the general reaction of the body tissues to invasion by the virus.

Outcome

(1) Appearance of second stage after 1-2 days.
(2) Recovery without further signs or symptoms.

Stage II

A different clinical picture becomes evident which seems to indicate invasion of the central nervous system (cerebral and spinal) by the virus:

(1) Stiffness of neck and back (positive spine sign).

(2) Facial expression of fear—wide open eyes, anxious expression, flushed cheeks.
(3) Hyperesthesia and irritability.
(4) Muscle pain.
(5) Occasionally tremor or ataxia.
(6) Occasionally mental confusion.

Outcome

(1) Recovery without paresis or paralysis (abortive type).
(2) Paralysis without a fatal outcome.
(3) Paralysis resulting in death.

The paralysis is either (1) a segmental, flaccid paralysis of spinal origin or (2) bulbar, with or without other paralysis.

The spinal type of paralysis usually shows a patchy distribution, but may be widespread. In severely paralyzed cases, the respiratory muscles may be involved.

The bulbar type occurs when the medullary centres are involved and is the most serious form of the disease. It is usually first recognized by a nasal tone to the voice or difficulty in swallowing, often resulting in fluid being extruded from the nose. The inability to swallow progresses and mucus and saliva accumulate in the throat. In serious cases, the patient becomes disorientated and comatose and death due to respiratory and/or circulatory failure is not an uncommon outcome.

Diagnosis and Spinal Puncture

The variable clinical picture produced by the virus is the basis for the diagnosis of the disease. Spinal puncture may serve as an aid in making the diagnosis.

The spinal fluid during the first stage is normal. That of the second stage has an increase in cells (lymphocytes) varying from 10-1000 but usually between 20-200. The globulin content is increased (Pandy Test). Cases have been reported with normal spinal fluid findings.

IV. Prognosis

During the acute stage, predictions as to the course of the disease are risky. There is no way to be certain that paralysis will not develop or if present will not progress. If paresis does develop it usually comes on early in the second stage and reaches its limit rapidly. However there is a smaller percentage of cases with slowly developing paralysis which may appear any time during the acute stage. As fever and other signs of acute infection recede, the danger of paralysis diminishes. Bulbar cases are the most serious—50% die. If paralysis does develop, the extent of recovery is also difficult to predict. Muscles not completely paralyzed have an excellent chance of improvement, from slight improvement to complete recovery. The chances for much improvement in a completely paralyzed

group of muscles are not good, but a remarkable recovery is not uncommon. If improvement has not occurred within two years, the paralysis is almost certainly permanent.

V. Treatment

There is neither a specific method of prevention of the disease nor a treatment which destroys the virus or prevents the onset and spread of paralysis.

The most important aspect of therapy in the acute stage is bed rest and careful nursing. Measures are taken to prevent stretching of involved muscles by gravity or unopposed opponent muscles. These measures include fracture-boards with foot-boards to prevent foot-drop, and light removable splints. Physiotherapy treatment is begun as soon as possible.

Miss Kenny has advanced a treatment which is highly regarded in some centres. She considers the flaccid paralysis mostly functional in origin and resulting from *spasm*. If one group of muscles is in spasm and cannot relax, the antagonist group is prevented from contracting due to the brake-like action of the spastic muscles. Any attempt to contract the non-spastic muscles stretches the antagonistic spastic muscles, increasing the pain and spasm. A fear complex is set up and the patient refrains from using the muscles, which causes a functional breakdown between brain-control and the non-spastic muscles resulting in a flaccid paralysis—so-called *mental alienation*. She also emphasizes *inco-ordination* which is caused by the substitution of uninvolved muscles for those with a moderate degree of spasm and flaccid paralysis. The movement is not smooth or co-ordinated.

Spasm is treated by continuous application of hot packs to the spastic muscles.

Alienation is treated by restoring the mental awareness of the alienated muscles by explaining the normal action of the muscles.

Inco-ordination is treated by teaching them to make the movements slowly and smoothly by repeated exercises, preventing muscle substitution.

It should be remembered that the Kenny theories and treatment are not universally, or even widely accepted.

Physiotherapy certainly plays a most important role in the treatment of the disease. Attention is paid to early deformities and their correction. Muscle training is stressed to prevent disuse atrophy and to aid in the restoration of function. This includes passive and assisted movements, underwater exercises, electrical muscle stimulation. Massage, baths and heliotherapy are also utilized.

There comes a time when muscle recovery reaches a maximum of improvement. Plans should then be made for reconstructive orthopedic surgery including tendon transplantations, fascial reinforcements, and joint-fixations.

Clinical experience makes it possible to recognize many more cases early in the infection—prompt isolation and treatment decreases the incidence and sev-

erity of the disease—adequate treatment prevents the development of serious deformity. Finally, continued physical therapy and judicious orthorpedic surgery enable many severely crippled persons to assume gainful occupations and a useful role in life.

The author wishes to thank Dr. Beverly Hannah for his great help in the preparation of this article.

REFERENCES

(1) Lewin, P.: Anterior Poliomyelitis.
(2) Howe and Bodian: Neural Mechanisms in Poliomyelitis.
(3) Wilson, J. L.: The Use of the Respirator in Poliomyelitis.
(4) Pohl and Kenny: The Kenny Concept of Infantile Paralysis.
(5) Hannah, B.: Symptomatology of Anterior Poliomyelitus: Symposium on Anterior Poliomyelitus Presented to the Academy of Medicine, Toronto, September 7, 1937.
(6) Boyd: Textbook of Pathology.

BETTER RADIOGRAPHS

R. H. JOHNSON 4T8

During the past few years, as more and more medical centres have obtained X-ray units, junior internes have been called on to take more and more of their own radiographs. The proper performance of this duty requires a basic knowledge of diagnostic films, X-ray equipment, and technique. However, few have the time to read the extensive literature on this subject. In this article it is proposed to gather together the gist of the material in a usable and readable form in order that the beginner and the expert may have a basic concept of, and a better ability to use diagnostic X-ray units.

To begin on familiar ground let us look at a radiograph. In observing it we look for four basic qualities, namely (1) density, (2) contrast, (3) detail, and (4) distortion. To be "diagnostic" the radiograph must have satisfactory density, sufficient contrast, maximum detail, and minimum distortion. These four qualities might be applied to any density chart, of which a radiograph is only one form. It represents the relative translucency or opacity of gross structures in the body to X-ray radiation. To be of use these differences must be accurately recorded.

Density, to deal with each quality individually, is an indication of penetration. Hence a film can be too dense as indicated by an all-over blackening, or not dense enough as indicated by an all-over whiteness. It is a matter of seeing what you wish to see, clearly in the middle colour range.

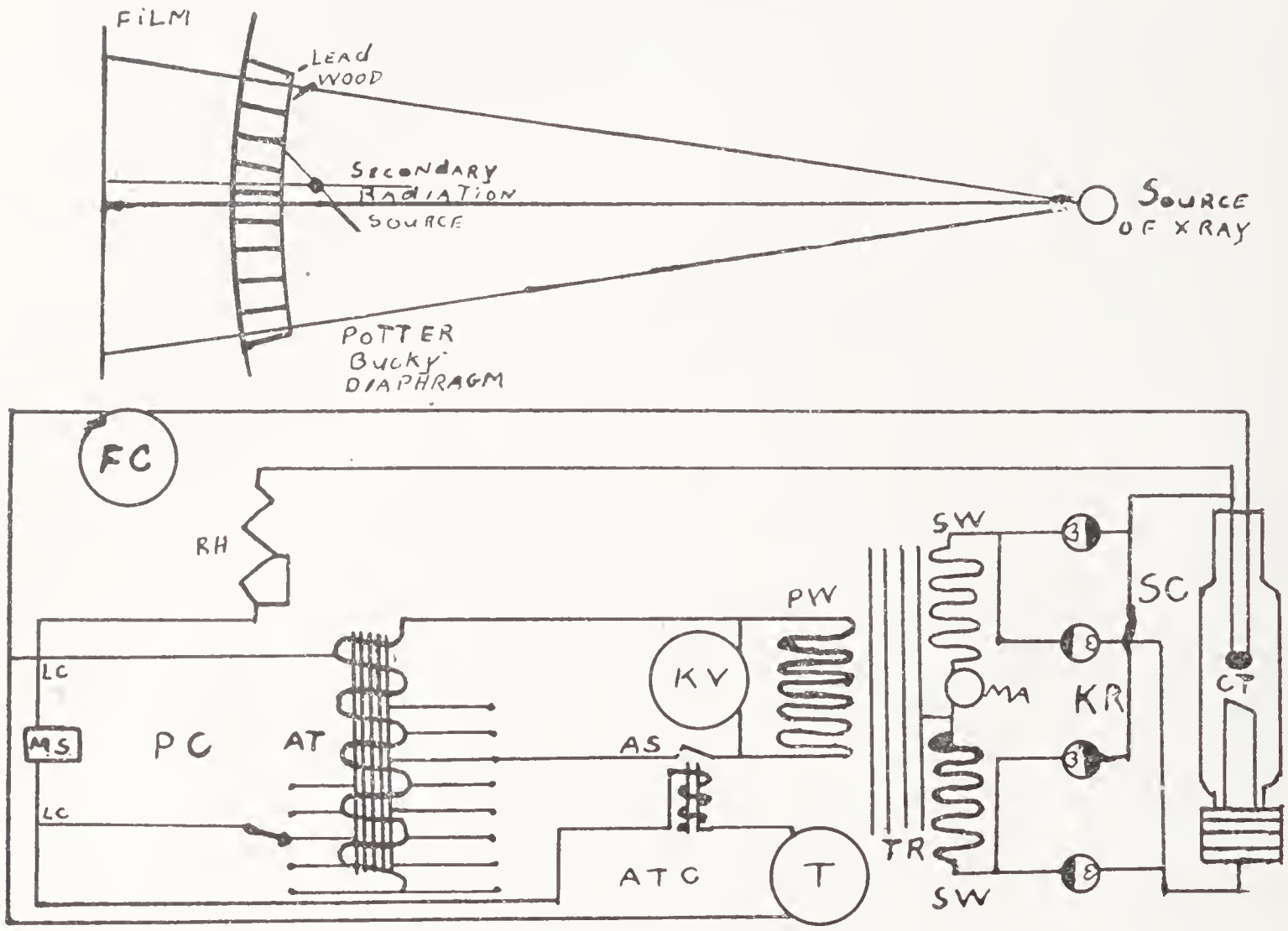
Contrast, in a radiograph, refers to the gradation from black to white, and the sharpness of this gradation. More specifically, it means that the border and detail of one radiotranslucent substance stands out more or less clearly against a background of a more radiotranslucent substance. If a film is too "contrasty" one structure fades into the next without a definite border; if there is not enough contrast one structure stares forth without any recognizable background. The diagnostic radiograph will have each structure sufficiently clearly outlined against its background.

Detail is the same in a radiograph as elsewhere. The finer structure of the part must be visualized. This is especially important in bone work where the pattern of the bony trabeculae must be unbroken if fracture is to be excluded, or in chest radiography where the detail of the lung markings is all important. Always maximum detail is desired.

Distortion is a deviation of the radiograph from the true representation of the part portrayed, due to projection and magnification. The best analogy is with shadowgraphy as practiced in the parlor. You will recall that using a point source of light and holding the hands in certain positions in relation to the light, silhouettes of rabbits and other animals could be cast on the wall. Similar results occur in radiography, but here the problem is to recognize from the shadow the object producing it. It is obvious that distortion must be kept at a minimum.

Now, knowing how to appraise a film, in the light of its four qualities, we must study the equipment used to produce the radiograph, and how the operator

controls the qualities of the resultant film by controlling his equipment The consideration of this aspect of radiology is best broken down into the consideration of the electrical circuits, the standard control panel, the table, the Potter-Bucky diaphragm, and the film.



The Electrical Circuit (See text)

The electrical circuits concerned in any X-ray unit are shown in the accompanying diagram, which, though not portraying the design used in any given unit, shows the basic circuits in their proper relation. As a detailed description is not possible in this article the details of this circuit are: that it is for a Coolidge hot filament tube, with two hundred and twenty volt line, controlled in the primary circuit by an autotransformer, with a full wave kenetron rectifier in the secondary circuit, a subsidiary timer circuit operating an automatic magnetic switch in the primary circuit, and a filament circuit. The parts traversed by the current are in order, referred to the diagram, the line circuit (L.C.), coming into the apparatus, with its main switch (M.S.). Then there is the primary circuit (P.C.), containing the autotransformer (A.T.), the automatic timer switch (A.S.), the primary winding (P.W.) of the transformer (TR.), and bridging the primary winding the voltmeter (K.V.). Next comes the secondary circuit (S.C.) containing the secondary winding (S.W.) of the transformer (TR.), the full wave kenetron rectifier (K.R.), the ammeter (M.A.), and the Coolidge tube (C.T.). Also shown are the filament circuit (F.C.) kept constant by a rheostat (RH.) and the automatic timer circuit (A.T.C.) with the timer (T.).

The standard control panel has the following indicators and controls, given in the order in which they should be noted when the unit is turned on. When the main switch is thrown the line indicator shows the constancy of the incoming current. It is adjusted to the desired value by a switch marked "line compensator" or simply "line," which should never be changed with the main switch on. The filament current is indicated on another dial marked "filament," which is controlled by a rheostat marked "filament" or is preset without a variable conrol. Then there is the amperage indicated on a milliammeter in milliamperes, one one-thousandths of an ampere. It is controlled by a switch marked "milliamperes," usually arranged to give set values of five, thirty-three, fifty, seventy-five, one hundred or two hundred milliamperes, a control not changed while the main switch is on. The voltage is indicated in kilovolts, thousands of volts, by a kilovoltmeter, and is varied by controls marked "auto-major" giving steps of ten kilovolts, and another marked "auto-minor" giving steps of one kilovolt. These can be changed with the main switch on. Finally there is the timer, which is marked in seconds, subdivided in tenths or even into fiftieths, and is indicated as the "time." It also can be changed with the main switch on.

There is X-ray opaque shielding about the tube with a window for the escape of effective radiation. Covering the window is a filter of one-half a millimeter of aluminium to filter out the radiation of long wavelength which might burn the patient. Also there is a place for cones.

The table set up consists of a table on which to place the patient or part to be radiographed, a tube stand or holder for the Coolidge tube, and a place beneath the table for a film with or without a Potter-Bucky diaphragm. The tube stand is designed so that the tube can be raised or lowered over the patient, usually from twenty to seventy-two inches. Cones are tubes of metal used to limit the area of tissue exposed to X-ray. The table has no unusual features except that if films are to be placed below it, it must be relatively radio-transparent.

The Potter-Bucky diaphragm, usually placed under the table, is a method of limiting the effects of secondary radiation. Secondary radiation is X-ray radiation produced in any matter struck by primary X-ray radiation from the tube, but unlike the primary rays it is not produced from one centre, but is produced from many centres and comes off in all directions from each centre. Naturally the end result is fogging and lack of definition in the film. To prevent this the Potter-Bucky diaphragm was designed. It consists of slabs of lead alternated with slabs of wood, the long sides of the slabs paralleling the primary rays from the Coolidge tube (see illustration). Any secondary radiation from the part being radiographed, if not travelling parallel to the primary rays, is trapped in the diaphragm, for, as it enters at an angle, it strikes the lead slabs and is absorbed, lead being radio-opaque. The primary rays and rays parallel to it pass through the wood. To prevent the lead strips leaving clear white lines on the film, the Potter-Bucky diaphragm is moved across between the patient and the film at the same time as the exposure is made. The moving lead strips leave no

mark. There is a switch to synchronize the time of the exposure with the movement of the disphragm.

The film and its handling now deserve attention. Film is of two main types, one-side emulsion and two-side emulsion. The one-side emulsion is little used at present, and it is mentioned only to say that care must be taken in loading it into holders in order that the emulsion be toward the source of radiation. The film with emulsion on both sides is the most popular. Care must be taken in handling it, however, as both sides soil easily from contact with moisture or dirt. Film is best when not touched, or when handled only by the corners. All film is light sensitive, is handled in the dark, and is packaged against light. In the darkroom it is loaded in light-proof holders of cardboard, or in cassettes. The cassette is a metal and plastic holder containing two screens of calcium tungstate crystals which fluoresce under the influence of X-ray radiation. Hence, unlike cardboard holders in which the film is exposed by X-ray only, in the cassette the film is exposed both by radiation and the light given off by the fluorescent screens. This means less time or less penetration is required for exposure. After exposure the film is again taken to the darkroom and, with the same care to avoid soiling or scratching it, is developed and fixed. The developers and fixers are bought from established firms, and the manufacturer provides for more accurate instructions for their use than can be given here. Speed of developing is governed by temperature, similar to other chemical reactions, and each manufacturer recommends an optimum temperature for his product. The developing procedure should be maintained the same for all films, and be such that the properties of the film emulsion be used to the best advantage. Overdeveloping will give a black film, underdeveloping will give a grey film.

We now have equipped ourselves with a basic knowledge of what constitutes a diagnostic radiograph, and of what equipment is used to take radiographs. It now remains to relate our technique in taking the film to the qualities desired in the resulting picture.

The beginner usually finds the instructions for taking the desired picture in a book or on a chart provided by the manufacturer. This is known as a "technique." It lists the procedure usually in the following order: cassette or cardboard holder, Potter-Bucky diaphragm or no, milliamperage, kilovoltage, time, and distance of tube to film. Commonly milliamperage and time in seconds is combined and listed as milliampere seconds (indicated as M.A.S.) because it is found that for any given exposure the product of the milliamperes times the time in seconds is constant. With this setting of his unit a picture is taken. The resultant radiograph is judged for its qualities of density, contrast, detail and distortion. The method of changing any one of these, or any combination of them, will be dealt with.

For this discussion certain abbreviations must be used. These are M.A. for milliamperes, KVP. for kilovoltage, T for time in seconds, and M.A.S. for milliampere seconds.

Density is controlled by four factors, two of which are varied in routine work. The variables are (1) Kilovoltage—an increase of ten KVP. doubling the density,

an increase of thirteen KVP. tripling the density, and an increase of sixteen KVP. quadrupling the density. This is because the increase in KVP. not only increases the amount of radiation, but it also changes the quality of the radiation so that it penetrates better. (2) Time—directly affects the density. The density is directly proportional to the time of exposure, doubling the time resulting in double the density. The fixed factors are (3) Milliamperage—which is set for the type of unit employed. The density varies directly as the M.A., a doubling of M.A. resulting in double the density. This relation is the same as that of time, hence the derivation of the constant M.A.S. for any given exposure technique. (4) Distance, that distance from the tube to the film,—the density varying inversely as the square of the distance. This relation is the same as the intensity of ordinary illumination at a given distance from its source.

Contrast is influenced by six factors, all of which can be controlled. (1) Kilovoltage—as the KVP. is increased the amount of secondary radiation increases disproportionately, and grey fogging results. KVP. must be kept high enough to penetrate the part being studied. (2) Potter-Bucky diaphragm as previously pointed out screens out secondary radiation giving greater detail. Its use requires an increase of KVP., nine for the old type, sixteen to twenty for the new high-speed type, or thirteen when in doubt, to penetrate the added thickness of the diaphragm. (3) Cones—cut down the amount of tissue radiated and hence the amount of tissues giving rise to secondary radiation. This directly affects the fogging of the film due to secondary radiation. (4) Screens in cassettes—in speeding up the exposure, or an an alternative allowing a reduction of KVP., reduce the secondary radiation produced and hence the fogging. (5) Development—overexposure and underdevelopment of the film spoils contrast, giving no absolute blacks at all. (6) Fogging of X-ray film due to age, heat or X-ray spoils contrast.

Detail is determined by five factors. (1) Focal spot, the size of the part of the target of the cathode tube struck by electrons and giving rise to radiation. Its size is determined by the ability to keep the metal from melting, hence the use of rotating anode tubes, and the use of small and large focal spots on stationary anode tubes. The object is to get as near a point source of radiation as possible, for the same reason as a small source of light is used in picture projectors. (2) Focal-film distance is a factor in the same way as in shadowgraphy, a point source at infinity casting a sharper edged and truer shadow than when closer than infinity. About seventy inches is the maximum economically practical distance. (3) Object-film distance is also important as in shadowgraphy, the closer the object is to the surface (film) on which it is projected, the clearer the image is. (4) Screens in cassettes place a limiting factor on the detail, the factor being the size of the calcium tungstate crystal. This crystal size is even greater when photographic spread of its fluorescence is seen on the film. (5) Movement will blurr the picture of the part making detail indefinite.

Distortion is determined by three factors. (1) Focal-film distance—the closer the focus is to the film the greater is the magnification of the part. This is best thought of as spread of the image as the source of radiation approaches the

film. (2) Object-film distance should be as short as possible for as the part gets farther from the film the magnification of the image increases. This is due to the cone-like spread of both the radiation from the focus and the shadow of the part, namely, of the object. (3) The alignment of the tube, object and film. To get the least distortion (best definition) the object, and film should be at right angles to the centre ray of the effective radiation from the tube. The study of positioning in radiography is designed to eliminate distortion. It is interesting to note that in taking radiographs of parts where distortion is inevitable, standard positions are used so that the distortion will be the same in normal radiographs, and comparison can be made to detect abnormal structure.

With a careful analysis of any radiograph and thorough knowledge of the foregoing material, it is easy to correct the setting of the X-ray equipment and take a second picture with qualities such that it is of diagnostic value.

It would be well for the person starting out to take radiographs which are to be read by a radiologist of an institution or of the Workmen's Compensation Board to take pictures of the quality desired by the radiologist. His likes and dislikes in the qualities decided by opinion, namely density and contrast, should be learned and respected. It is also helpful when handling radiographs to remember that the American Medical Society has ruled that the radiograph is the property of the radiologist, and is available only to the patient's doctor, or a doctor called in as a consultant, not to the patient.

In concluding this article the interested reader is referred to the excellent books on the subject of Radiographic Techniques and Positioning, a few of which are: Medical Radiographic Technic, prepared by the General Electric X-Ray Corporation and published by Charles C. Thomas; United States Army X-Ray Manual, 1919; Principles of Radiographic Technique by Santé; Roentgen Technique by Clyde McNeill, M.D., published by Charles C. Thomas; and Positioning in Radiography by K. C. Clark, published byLondon Ilford Limited.

THE ROLE OF THE OVARY AND PITUITARY IN SEX FUNCTION

By D. J. RAE

Part 1—Historical Background
Part 2—Pregnancy
Part 3—The Menopause

Part 1

Historical Background

Only within the past hundred odd years has any significant work been done to assist in the explanation of menstruation and pregnancy.

Before the work of Pflueger in 1863, both the laity and medical practitioner had grossly distorted conceptions regarding these functions. The folk-lore regarding menstruation was such that it was considered a periodic purging or cleansing of the woman's body. As far-fetched as this may now seem, many of us as practitioners, will undoubtedly be confronted by many patients who adhere to this belief.

The beliefs maintained by the medical profession were not much more advanced, the more important being:—

1. The plethora theory of Galen which stated that all women were naturally plethoric and so menstruation was a periodic blood-letting facility.
2. The theory of Democritus—who suggested that menstruation was due to a ferment which brought about a boiling over of the blood so that menstruation resulted. This ferment was given the name 'fervor uterinus'.
3. The lunar theory—which postulated that menstruation was related to the cycle of the moon because of the similarity of cyclic periodicity. If this was considered from a broad viewpoint, that is, that the sex cycle of the woman was influenced by natural environmental phenomena, including even the cycle of the moon, the theory had more basis than some of its predecessors.

The important common feature of these theories is that none at any time suggested a relationship between menstruation and the presence or function of the ovaries.

Outstanding work in this field was done by the following workers:—

1. *Pflueger*

He was the first to ascribe the cause of menstruation to the function of the ovaries in a well-defined theory. It was his belief that a pelvic hyperemia was caused reflexly by the nervous system because of an influence from the developing Graafian follicle of the ovary. This view was fairly well accepted and was taught until the end of the 19th century.

2. *Knauer*

Pflueger's theory was proved incorrect by the transplantation studies of Knauer. He showed that excision of the ovaries interrupted the cycle while their transplantation to some other part of the body re-established it. These experiments proved that the nerve connections of the ovaries were not concerned in the production of the cycle, but that the influence must be through an internal secretion into the blood stream.

This was the beginning of the present day hormone theory of menstruation, a concept which began to take hold and for which a very simple explanation was at first offered, that was that the phenomenon was caused by the internal secretion of the ovaries, but what the secretion was or its source were unknown.

3. *Frankel—1903*

Frankel made the next contribution by demonstrating the endocrine importance of the corpus leuteum which had hitherto been considered merely the functionless end-product of the ruptured Graafian follicle.

4. *Hitschmann and Adler—1908*

Work was immediately begun on the life history of the follicle and corpus luteum so in 1908, when the work of Hitschmann and Adler was brought forth on the histological cycle of the endometrium, an immediate co-relation was possible between the ovarian and endometrial cycles.

Subsequently a satisfactory concept of the sequence of histological events during the menstrual cycle was made, which it has not been necessary to change in any fundamental way since.

5. *Papanicalaou and Stochard—1917*

These workers made the problem a laboratory as well as a clinical study by recognizing that the vagina of animals as well as the uterus underwent definite cyclical changes.

6. *Doisy and Allen—1923*

Doisy and Allen furthered this work by demonstrating that the chronology of the sex changes could be conviently and accurately studied from smears of the vaginal secretions.

Since then the work has rapidly progressed.

The Ovarian Hormones

In 1917, Frankel made a short report on the estrous producing effect of a hormone contained in the follicular fluid but the credit goes to Allen and Doisy who in 1923 demonstrated the effects of this hormone.

At first many names were given it, such as Folliculin, Female Sex Hormone, Estrin, Theelin, Menformon, and others. After Zondeck showed that it was present in large quantities in the urine of pregnant women, the isolation was greatly facilitated and finally accomplished in 1929 by many workers almost

simultaneously. We now know the mollecular structure and a number of derivatives, more or less estrogenic, have been demonstrated.

1. Estradiol—which is believed to be the estrogenic principle actually manufactured in the ovary.
2. Estrone—which is the form found in largest amounts in the urine, and
3. Estriol and Estradiol which are present in the urine.

It was thought that two separate ovarian hormones must exist because of the histological endometrial changes.

In 1929, Corner and Allen established the presence of a hormone principle in the corpus luteum. Shortly afterwards a crystalline form was again segregated by various groups of workers and called 'Progesterone'. Its chemical formula as well as that of several derivatives is not known.

In 1937, Venning and Browne demonstrated the substance excerted in the urine as the excretion form of progesterone and called it 'Pregnandial'.

The Pituitary Sex Hormones

Although there was a time when menstruation was looked upon as a pelvic phenomenon involving the uterus and ovaries alone, we now know that organs and tissues far removed from the pelvis are involved. Menstruation is only one manifestation of this cycle, the real purpose of which has to do with reproduction.

Frohlich—1903

Since the work of Frohlich in 1903, it has been known that the pituitary is linked up with reproduction in both male and female, but the relationship was a mystery until recent years.

The methods of studying the problem were:

1. The ablation method, and
2. Injections of pituitary extracts—these were used but results were confusing and conflicting.

It was not until 1926 that a new approach to the problem was devised by one Smith and Engle, and secondly Aschheim and Zondeck. The basic idea of their studies was the effect of implantation of pituitary tissue in amimals. By these methods it was clearly established that the anterior lobe of the pituitary exercises hormonal dominance over the ovaries. This control depends upon the production of two gonadotropic principles:

1. The follicle stimulating hormone which is responsible for the maturation or ripening of the Graafian follicle and thereby the motivation of estrogen.
2. The luteinizing hormone which is responsible for the luteinizing changes in the ovary and so the production of progesterone.

This relationship is a reciprocal one, the gonadtropic function of the anterior lobe being inhibited by large amounts of estrogen and vice versa.

The isolation of the gonadotropic principles of the pituitary has not been possible and we know nothing as to their chemical structure. Any prepared extract is impure, always containing certain amounts of other pituitary hormones

and always with a certain amount of protein material. Many other hormones have their origin in the anterior lobe but we are not concerned with these at this time. The only important factor seems to be the questioned multiplicity of hormone principles. Many endocrinologiests now seem inclined to the belief that these varied effects may be produced under varying conditions by a much smaller group of cardinal hormones, perhaps only three or four in number.

From this brief historical review it can be seen that the field is relatively a new one; that much outstanding work has been accomplished; but that a great deal is still unknown and much more investigation is required to give a complete understanding of the subject.

Part II

Hormones of the Pituitary and Ovary in Pregnancy

The first hormone of interest is the follicular stimulating hormone which is supposedly produced by the basophilic cells of the anterior lobe. This follicular stimulating hormone acts upon the primordial follicle of the ovary to stimulate its growth. This maturing follicle produces the hormone 'Estrogen' which produces the characteristic growth effect upon the endometrium, i.e. the glands undergo an increase in size and tortuosity, an increase in thickness and there is a relative hyperemia of the mucosa. There is no evidence, though, of secretory activity at this time.

By the mid-interval period, ovulation occurs, but the factors determining the rupture of the follicle and extrusion of the ovum are still unknown. Available evidence seems to indicate that ovulation is determined by a delicate quantitative balance between the follicle-ripening and the luteinizing hormone, presumably a large quantity of the former and a small amount of the latter. The determining factor in the production of the luteinizing hormone is also unknown but it seems that it is due to an increased amount of estrogen.

After the follicle has ruptured a temporary drop in estrogen production occurs. This causes a temporary retrogression in the endometrium so that not uncommonly slight intermenstrual staining is seen at this time.

Activity is now begun by the action of the luteinizing hormone of the pituitary upon the corpus luteum as it develops from the collapsed follicle. Increasing production of progesterone occurs due to rapid luteinization of the granulosa by the activity of this hormone. Estrogen does continue to be produced by the corpus luteum.

Characteristic changes occur in the endometrium, the result of progesterone activity upon it. There is increased thickness and oedema, increased tortuosity of the glands, steadily increasing secretory activity of the glandular epithelium and decidua-like hypertrophy of the stromal cells.

Up to now this has been merely the build-up of the endometrium as in the pre-menstrual phase. Everything has been prepared for the reception and nidation of the egg in the event that the latter should be fertilized. If such occurs increasing amounts of progesterone continue to be produced by the corpus luteum

and the endometrium is not cast off but develops further becoming the decidua of early pregnancy. Definite evidence is forthcoming but it is felt that the corpus luteum of pregnancy continues to produce progesterone for only about the first three months, thereafter the production is probably by the trophoblast of the developing embryo. This is an important factor because it is at this time of transference of production of progesterone by the corpus luteum to the trophoblast that spontaneous abortion is most apt to occur. Recent studies by Heckel and Allen seem to indicate that the important function of estrogen is the maintenance of progesterone and that it is not the accumulation of estrogen but rather the withdrawal of progesterone that is responsible for the onset of labour. That the ovaries play only a small part in estrogen production is proved by the fact that ovarectomy in the early months of pregnancy makes little appreciable effect on the hormone level as measured in the blood and urine.

The hormone found in the urine of pregnant women which was formerly believed to be produced by the anterior pituitary and which is similar in many respects to the follicle stimulating hormone is now known to be entirely different and has been more properly termed the chorionic hormone, since it is also produced by the placenta. It is upon the presence of the chorionic hormone of pregnancy urine that the A.Z. test depends. If a trophoblast is living and functioning, and if the hormone has access to the maternal circulation, the A.Z. test will be positive. The greatest concentration of these hormones in the urine appears to be at the third to fifth month. Following this, there is a gradual decline towards the end of pregnancy.

Parturition

No definite proof exists that parturition is initiated by an endocrine mechanism. Until recently, as previously mentioned, it was thought that increasing estrogen might cause an increasing irritability of the uterine musculature, and an increasing sensitivity to the oxytocic principle of the posterior pituitary lobe, thus initiating strong contractions.

The recent experimental work of Heckel and Allen does not support this view. They demonstrated that the continued administration of estrogen prevents parturition by maintaining the function of the corpus luteum while degeneration of the latter is followed by parturition.

The conclusion drawn by these two men is that if parturition is caused by a hormonal action, it may be due to aging of the placenta with a subsequent drop in estrogen and progesterone levels. This would follow since progesterone production is mostly carried on by the placenta after the third month.

A substance thought to be a hormone active in causing relaxation of the pelvic ligaments during pregnancy was described by Hisaw in 1926. He called it 'Relaxin'. It has since been found in the blood of several species of pregnant mammals, in extracts of rabbit placentae, and in the corpus luteum of the sow.

The part, if any, that it plays in pregnancy is not known. However, relaxation of the pelvic joints does occur so perhaps further investigation will disclose a relationship.

Part III

Hormone Activity at the Time of the Menopause

The cause of the vasomotor symptoms at the time of the menopause is a cessation of ovarian function. It is known that if the ovaries are overactive that the pituitary function will be diminished or abolished and that as ovarian function is diminished or abolished, pituitary function will increase. These various effects are reflected in the study of the urinary hormones and so can be watched under different conditions.

At the menopause, there is an absence of marked deficiency of the estrogenic hormones with a corresponding increase in the gonadotropic principles. Much discussion has arisen as to the primary cause of the menopausal syndrome, that is, whether the ovarian deficiency or pituitary excess is the responsible factor. It has been established that cessation of ovarian function is the primary break in the normal balance. The ovary itself has a definite life span which ends at the menopausal epoch. Beyond this, no amount of pituitary hormone will reactivate it. At the same time there is good evidence to believe that the secondary pituitary disturbance is the immediate factor involved since the pituitary region is known to be the chief tie-up between the endocrine system and the higher nervous system.

PATHOLOGICAL PROCESSES OCCURRING AS A RESULT OF ACUTE HEAD INJURIES

NORMAN C. DELARUE, B.A., M.D.,

Part I

In order to formulate principles of diagnosis and treatment in acute head injuries it is essential that one appreciates the pathological changes that occur when the skull and brain are subject to trauma and the following brief review is presented with this object in mind. The features to be discussed are enumerated below:—

1. Methods of production of fractures of the skull.
2. Methods of production of injuries to the brain.
3. Fundamental pathological changes occurring as a result of brain injuries:
   (*a*) Contusion
   (*b*) Laceration
   (*c*) Cerebral trauma without contusion or laceration.
3. Repair of contusions and lacerations.
5. Secondary pathological conditions associated with head injuries.

Methods of Production of Fractures of the Skull

Linear Fractures

When force is applied to the head it tends to continue in the same direction in which it is travelling, but one cannot predict with accuracy its actual course as skulls vary so much in consistency, and there are strengthening buttresses both in the vault and in the base which tend to deflect the force along the line of least resistance. Therefore fractures tend to follow a zig-zag path and only those associated with overwhelming force willl cross such buttresses as the petrous ridge which commonly reflects the force, depending upon the direction in which its surface is struck, medially towards its apex or laterally towards its base. Foramina and fissures are weak spots and are readily traversed by the force, causing the fracture line to pass irregularly from one to another. Due to the fact that the basal buttresses radiate from the central pituitary fossa it is common to find fractures involving this region.

Basal fractures are particularly important as they are often associated with more severe injuries, and Rowbotham (1) states that they may be produced in four ways:—

1. Force applied directly at the level of the base of the skull.
2. General distortion of the skull wherever the forces are applied.
3. Extension from the vault.
4. Force applied to the base through either the spinal column or the face.

This latter method merits further discussion due to its common occurrence. Blows on the chin may occasionally fracture the glenoid fossa but the mandibular condyle is rarely driven into the cranial cavity as closure of the jaws transfers the

force to the face and prevents the mandible from moving upwards. The maxillary antrum crushes readily and absorbs a large amount of the force but the internal angular process is strong and readily transmits forces to the non-resistant cribriform plate which is easily fractured. This fracturing results in rupture of the olfactory filaments and loss of the sense of smell, and more importantly dural laceration with the danger of meningitis if the laceration of the meninges is sufficient to cause a cerebro-spinal fluid rhinorrhoea, the treatment of which presents a specialized problem and will be discussed later.

Gurdjian (4), using what he has termed a "stress-coat technique," has recently demonstrated very neatly the lines of stress along which these fractures tend to pass.

Depressed Fractures

These fractures occur as a result of local deformation of the calvarium, in which the outer table is compressed by the application of a localized force with consequent stretching of the inner table, this excess strain causing the inner table to fracture first. If the force is not of sufficient duration or severity, the outer table may remain intact. In this way, fractures of the inner table occasionally remain unrecognized, despite the fact that they may be of sufficient degree to cause dural penetration and local laceration of cerebral cortex. At operation these areas may be suspected when one discovers a bluish discoloration of the intact outer table subjacent to a scalp laceration and of course their presence is easily verified by radiological examination.

It is obvious, of course, that when a force is applied to the head causing acceleration of the cranium, a tremendous strain must be thrown on the strong ligamentous attachment of the skull to the atlas and axis, and it is not surprising that Brown and Russell (5) have proven experimentally that petechial haemorrhages are particularly liable to occur just beneath the piamater in the upper segments of the spinal cord and that this reaction is not an uncommon complication in cerebral trauma, occasionally reaching a degree sufficient to represent the primary cause of death or disability.

Method of Production of Brain Injuries

The brain may be injured in one of two ways:—1. Distortion of the skull or the so-called "compression" type of brain injury. 2. Movement of the brain in relation to the skull or the so-called "acceleration" type of brain injury.

Compression Type of Brain Injury

In distortion of the skull, the brain may be injured in two ways; either by the impact between the skull and the brain, which varies with the elasticity and architecture of the inner surface of the bone in the region to which the force is applied, or as a result of the rebounding of the skull on the release of force which causes haemorrhage and damage to the underlying cortex due to the fact that meningeal vessels are pulled away from the brain tissue. It should be realized that this is an uncommon cause per se of brain injuries resulting in unconscious-

ness, because it has been proven experimentally that to produce unconsciousness by crushing alone, requires a deformity of such degree that the intra-cranial pressure exceeds the systolic blood pressure.

Acceleration Type of Brain Injury

This type of injury is associated with more severe effects, as the movement of the brain in relation to the skull causes stretching of fixed structures and possible rupture of nervous pathways or blood vessels. As Rowbotham (1) points out, the damage is most likely to occur in areas where the cerebro-spinal fluid cushion does not support the cortex, this preventing its contusion against the resistant bony framework of the skull. Accompanying this displacement of the brain and its contusion against the skull, there is an associated zone of diminished pressure in the region left vacant by the movement of the skull when it is subjected to rapid acceleration or by the movement of the brain when motion of the skull is rapidly decelerated and the resulting suction may cause rupture of superficial and occasionally deeply placed vessels. Holbourn (6) has suggested that the fundamental cause of brain injuries is the production of a "Shear strain" dependent upon the rotary acceleration imparted to the skull content by a force applied to it. Distant damage to brain tissue is explained on this hypothesis as the result of rotation of cerebral tissue around regions where the brain is fixed in relation to the skull such as the falx cerebri and the tentorium. This "shear strain" imparted to the brain tissue may cause organic lesions or produce symptomatology and nervous manifestations as a result of a "pulling apart" of the constituent particles of the cerebral tissue in Holbourn's opinion.

Contre-coup injuries

It has long been recognized that blows on the occiput, as, for example, in a fall on the back of the head, are frequently associated with lesions of the brain in the frontal and temporal poles, and that the application of force to one side of the head is apt to produce a similar lesion over the temporal pole on the opposite side. The term "contre-coup-lesion" has been applied to this group of injuries and many theories have been advanced to explain its causation. Moritz (7) suggests that the energy of impact is propagated by waves which diverge as they leave the point of impact and converge as they approach the opposite pole, this divergence dissipating the energy during its passage through the central portion of the brain and the subsequent convergence re-focusing and intensifying the energy, again resulting in a "contre-coup-lesion". Others have suggested that when the brain belatedly picks up the acceleration induced by the force initially acting, the moving surfaces of the brain are brought to rest by the contralateral surface of the skull thus imparting a lesion by contusion. Ritchie Russell (8) believes that traction rather than contusion is the important factor, explaining the sub-arachnoid bleeding on the basis that the brain, having a different specific gravity than the skull, does not undergo acceleration as rapidly as the skull and consequently a zone of negative pressure is induced on the surface opposite to the point of application of the force. This undoubtedly is an explanation of

many cases of rupture of communicating vessels but does not seem to satisfactorily describe the causation of extensive lacerations of both cortex and membranes which are so prone to occur in these injuries. The definite preponderance of contre-coup lesions of the frontal and temporal poles, is explained by the absence of spinal fluid cushions in these regions as compared to the occipital poles and cerebellum which are almost never involved in a fall on the frontal region.

Fundamental Pathological Changes Occurring as the Result of Brain Injuries

As has been already pointed out, the brain may be injured in two definite ways during the period in which the force is acting and pathologically these changes are exhibited as contusions or lacerations. In addition, a lesion may occur of sufficient degree to cause definite changes in the level of consciousness without any apparent organic evidence of brain damage, although there is a growing tendency to suspect that with improvement in histo-chemical technique, the great majority of these cases will subsequently be found to have a demonstrable cellular pathology.

Contusion of the Brain

Contusions are commonly superficial in position, tend to be wedge-shaped, small in size, and are associated with petechial haemorrhages. Rowbotham (1) describes the microscopic changes as consisting of extravasted blood arising from ruptured vessels or from diapedesis in response to the damaged brain cells which surround the area of haemorrhage. These punctate haemorrhages often possess a perivascular distribution and are termed "ring haemorrhages". In the zone immediately adjacent to this haemorrhage, the neurones, glial cells and microglia are completely destroyed with demyelinization and breaking down of axones while more peripherally the staining properties and the shapes of the cells are altered so that one cannot state whether the injury is permanent or not. Acute swelling of the oligodendroglia is an early and consistent feature at the periphery. Surrounding this whole region there is an area showing hypertrophy and increase in number of the astrocytes and microglia from which zone phagocytosis and repair is initiated. It is important to realize that these areas of contusion contain not only cells that have been frankly destroyed but also cells which are on the border-line of necrosis and which may recover under ideal conditions but which will succumb if the blood supply is further imapired by secondary increases in intra-cranial pressure. Thus in patients who recover from the initial effect of the trauma, the prevention of secondary pathological conditions which might adversely effect the progress of these damaged cells, forms the basis of successful treatment.

Laceration of the Brain

This type of lesion tends to occur in the regions in which contre-coup injuries are produced, and is usually superficial in distribution, deep lacerations being

lacerations associated with displaced fractures. The piamater is invariably torn and therefore sub-arachnoid bleeding is common and may be diffuse. The arachnoid is also usually torn and blood and cerebro-spinal fluid may collect under the dura but it is important to realize that the dura is a tough structure that rarely gives way in this type of lesion and therefore, as we shall see later, there is a minimal danger of post-traumatic epilepsy developing as a result of the healing process. The cellular changes are the same as those occurring in contusions but are more extensive and severe.

Cerebral Trauma Unassociated with Contusion or Laceration

Although Brown and Russell (5) have shown that concussion can be caused by the forces of acceleration alone, and the resulting neurological state be of a non-structural type which suggests that the brain can receive a purely non-structural physiological injury sufficient to produce diffuse neuronal changes and resultant alteration in the level of consciousness, most recent observers are embracing the opinion that the lesion is essentially an anatomical one and will be solved by advances in microscopy (Rowbotham) (1) or in histo-chemical study (Tedeschi) (9). Groat, Windle and Magoun (10) have shown, in experimental concussion, that there is a differential chromatolytic change in certain interneurone systems of the brain stem and other cytological changes in the pyramidal cells of the motor cortex, whereas the primary motor neurons of the cranial nerve cells are not affected. Hyde (3) reports that the intimate molecular structure of individual nerve cells of the brain is affected, apparently resulting in the accumulation of the lipoid in the brain into microscopically visible fat droplets, under which circumstances all nervous activity of the brain cell ceases. White and his associates (11) have pointed out that experimentally even a brief concussion causes an increase in the brain volume up to 5.5% and state that extravasation of blood through the capillary wall has been found to be the only factor involved and not of sufficient degree to cause histological changes. Penfield (12) has shown the presence of nerve fibres in the walls of intra-cerebral vessels and suggests that trauma may interfere with the normal vasomotor function resulting in a state of statis, oedema and anoxemia, causing organic damage secondarily. Many years ago, Trotter (13) originally demonstrated the fact that mechanical stimulation of a pial vessel experimentally would cause it to constrict and this might be the basis of injury in distortion of the skull, causing an anoxemic state progressing to organic damage as above. Rowbotham (1) firmly believes that demonstrable changes in the neurone other than in the contusional areas can always be found following fatal injury, particularly if the patient has survived more than 24 hours and suggests that in fatal cases of cerebral trauma, widespread vascular changes are often found, with the capillaries as well as the venules sharing in a general congestion which indicates that the vascular changes are the result of active participation of the vessel walls in this state rather than the consequence of pure mechanical obstruction due to increased intra-cranial pressure. He believes that these changes are fundamentally important and points out that it is well recognized that stasis can produce small foci of softening in cerebral

tissue. Undoubtedly recent reports are emphasizing the frequency with which organic lesions are to be found in cases which in the past have been relegated to the group in which no anatomical cause for the change in the state of consciousness could be discovered and improvements in technique are liable to lead to stimulating advances in the future.

Repair of Contusion and Laceration

The repair of damaged areas of brain tissue occurs as a result of identical processes to be observed elsewhere in the body, comprising initially a stage of autolysis followed by phagocytosis of necrotic material and its eventual replacement by a type of granulation tissue, the disposition of which depends upon the degree of initial trauma. The phagocytosis of autolysed material is carried out by the micro-glia which invade the zone of necrosis, and during the active phas become swollen and granular and are known as "Gitter" cells. This stage is followed by a condition known as "gliosis" in which there is a peripheral hypertrophy of astrocytes which migrate into the wound, and as Linell (14) points out, a subsequent felting of the astrocytic processes with disappearance of the cell bodies and the formation of a firm glial scar may be the final stage of healing when no gross loss of cerebral tissue has occurred. However, where there is a gross loss of tissue, the final healing is brought about by fibrous tissue which grows in from the periphery as granulation tissue in the usual manner. This mesodermal activity is particularly marked if the lacerations are on the surface of the brain and are associated with membranous tears, for the proliferation of mesodermal elements has been shown by Penfield (15) to arise from neighbouring blood vessels and particularly those on the surface of the brain. This fact explains why so many scars are attached to the leptomeninges and why these scars tend to favour the sequela of post-traumatic epilepsy.

These brain scars may be attached to the dura, in which case they appear as a greyish gelatinous mass of tough and resilient consistency, or be free from dural adherence, when the overlying subarachnoid has not been torn, in which case they are represented by a depression on the surface of the brain, the floor of which is composed of shrunken gyri stained by yellow pigment.

Feature

R. K. GRAHAM, Editor

Quid dubitas?

MALCOLM H. V. CAMERON

Three hundred years ago a professor in Oxford greeted his classes with the question quoted above. The responses are not recorded. It is quite probable that many young men were shocked. They were looking for certainties of knowledge and were willing to accept the substance of a lecture as unassailable truth. It is also quite probable that many colleagues of the professor were more or less critical of the idea that a student might properly suggest that a grain of salt be taken with the bolus he was given to swallow.

We have historical proof that a goodly number of students of that day accepted the challenge. "The New Philosophy" was making its way against the authority of Aristotle. Willis described his "circle" about that time and Robert Boyle was seventeen. Newton was four years of age. The "Invisible College" had organized and was to become the Royal Society in 1662. We may well imagine that professors were faced with hard questions. The answers were very often similar to that given the baby elephant child in Just So Stories when he asked everybody "What does the crocodile have for supper?" Finally he was told, "Go to the banks of the gray, green, greasy Limpopo River and find out." He had to go alone but in Oxford, three centuries ago, the teacher frequently went along with his enquirer.

It is no compliment to a clinician if a student "takes notes without taking thought." Such a student pays no compliment to his own intelligence. Every good clinician hopes that he may some day shine with reflected glory because he has taught and perhaps inspired a great leader. Only doubters break from tradition and open new highways for the advance of science. Happy the student who finds himself assigned to the clinician who greets himself and his class every morning with "quid dubitas?"

Abstracts

E. R. YENDT, Editor

MEDICINE I

BENADRYL AS A THERAPEUTIC AGENT IN THE TREATMENT OF THE COMMON COLD. J. M. Brewster: Naval Medical Bulletin *47*, 810-811 (1947)

Benadryl was used by the author for the treatment of well over 100 cases of the common cold uncomplicated by bacterial infections of the respiratory tract. It was found to abort completely 10 per cent of such cases and to shorten the course and to afford marked subjective relief to 95 per cent of all cases. It did not prevent secondary sinus infection where the cold had become fully developed. The treatment in each case was ultra-conservative and consisted of 50 mgm. of benadryl and 10 gr. of aspirin taken immediately upon the onset of such symptoms as the individual recognizes as being those of a developing cold such as the engorgement of the nasal mucous membranes or soreness in the nasopharynx. In a few cases, the dose of benadryl was repeated in 24 hours.

It is concluded that benadryl is the most satisfying single therapeutic agent for the treatment of the common cold of virus origin. Its effects, which make the drug useful for such a purpose, include: (*a*) inhibition of the serous discharge from the respiratory mucous membrane to a degree equal to that of a conservative dose of atropine, (*b*) sedation equal to that produced by a therapeutic dose of phenobarbital, (*c*) inhibition of the cough reflex, perhaps because of the elimination of postnasal dripping, (d) abortion of herpes. Owing to the sedative effect, the patient should be cautioned against driving an automobile or doing any form of dangerous work.

W. G. B. C.

SURGERY I

THYMECTOMY IN THE TREATMENT OF MYASTHENIA GRAVIS. R. Adams and Frank N. Allan: Diseases of the Chest, Sept.-Oct., 1947.

Myasthenia Gravis was almost always fatal before the introduction of prostigmine. This measure is, however, only palliative.

Autopsies on cases of myasthenia gravis revealed thymic abnormalities in 47 per cent, of which a high proportion were benign thymomas. Thymomas, however, have been found without evidence of myasthenia gravis in the patient's history.

The first successful thymectomy was performed in 1939. Since then 129 cases of thymectomy in myasthenia gravis have been collected. Of these 17 are essentially well, 24 considerably improved, 27 moderately improved, 2 slightly improved and the remainder unclassified.

Before thymectomy is undertaken an accurate diagnosis must be established. This disease is characterized by marked muscular weakness beginning in the eye muscles with ptosis and strabismus, followed by disturbances of speech, swal-

lowing, mastication and finally a generalized weakness depending on the severity of the condition. The weakness is brought on by exercise and disappears or decreases with rest. Injection of prostigmine intramuscularly improves the patient.

Medical treatment should be undertaken for six months before surgery is considered. Twenty-five mg. of ephedrine are given twice daily along with the 2-25 fifteen mg. tablets of prostigmine each day as required. In most cases this will eliminate the symptoms or cause marked improvement. The group who are not relieved by medical treatment may turn to surgery for further help.

Because of the magnitude of the operation of thymectomy, critically ill patients in respiratory distress, mild cases, and patients over 40 years of age are not suitable risks.

Thymectomy does not cure myasthenia gravis but affords improvement, in many cases marked, in about 68 per cent of patients so treated. It is indicated in those whose disease continues to be severe and disabling after adequate medical therapy has been carried on for at least six months providing there is no contra-indication.

J. S. L.

SURGERY II

HYPERPARATHYROIDISM. G. H. Stobie: J. Can. Med. Assn. *57*, 233, Sept., 1947.

Stobie draws attention to this clinical entity as one which is being made less rare as the profession becomes increasingly aware of it; at the same time he points out that two relatively late manifestations of the disease are still generally being taken as inevitable requirements for its diagnosis. These late occurrences,viz., marked skeletal involvement and renal complications, could in fact be prevented by early surgical treatment. This will be possible only when the alert physician carries out the laboratory studies essential to the diagnosis in those patients who complain of generalized aches and pains or symptoms suggesting hypercalcemia.

The symptoms produced by the chemical changes in the blood per se are listed by Stobie as: muscular atony, weakness, fatigue, constipation, anorexia, weight loss, nausea and vomiting, polydipsia and polyuria. Very early skeletal changes produce minor generalized aches and pains.

If, on repeated blood examinations, hypercalcemia, hypophosphatemia and hypercalcinuria are found to exist in a patient with such clinical findings and who has adequate kidney function, one is justified in recommending exploration of the parathyroids even in the absence of demonstrable bone or kidney change.

J. H. M.

SURGERY III

FROSTBITE. PHYSIOLOGY, PATHOLOGY AND THERAPY. K. Lange, D. Weiner, and L. J. Boyd: New Eng. J. Med. *237*, 383 (1947)

Gangrene following exposure to cold air or constant cooling in dry surroundings (frostbite) was seen commonly in wartime and is not infrequent in civilian life.

The authors illustrate how, just prior to freezing, the red-cells clump together into occlusive masses which later undergo hyalinization. Due to the markedly increased capillary permeability, there is a rapid loss of plasma to the tissues. Within twenty-four to forty-eight hours, clotting occurs in the blisters formed, and it is assumed that a similar process occurs in the interstitial spaces giving rise to subsequent fibrosis and deposition of collagen.

In controlled animal experiments, they found that intravenous heparinization within twenty-four hours of exposure and continued for seven to nine days prevented the formation of the red-cell masses, and the gangrene which occurred in the controls did not result. Also, the fluid in the blisters remained in a liquid state and was resorbed.

Either cooling the exposed part or warming it to 44°C. for twenty-four hours after exposure increased the severity of the lesion. Cooling was the most harmful, and, although it delayed the blister formation, this was even more severe when it did occur. Room temperature seemed best.

Gangrene was prevented by these workers in fifteen human volunteers, though damage to motor and sensory nerves still occurred.

The authors describe two cases of frostbitten patients heparinized for five and seven days respectively both of whom escaped certain gangrene and loss of tissue.

R. H. S.

SURGERY IV

AETIOLOGY, DIAGNOSIS AND TREATMENT OF PROLAPSED INTERVERTEBRAL DISC. Quarterly Journal of Medicine, Vol. XVI: *63*. July, 1947.

As the background for the presentation of an exhaustive clinical account of prolapsed intervertebral disc the authors begins with a summary of the causes of sciatic pain and their relative proportions in his series of 305 cases. He divided them as follows: Group I—Prolapsed Intervertebral Disc, 53%; Group II—Diseases of the Myofascial Structures, 36%; Group III—Miscellaneous, 7%; Group IV—Psychogenic, 4%.

Symptoms of Disc Protusion—The usual sequence was: Initial trauma—onset of pain in back—onset of pain in leg. The characteristics of each stage were: Initial trauma—either a fall in spinal flexion or heavy-lifting in circumstances of mechanical disadvantage; back pain—a dull deep aching aggravated by sneezing, coughing, movement (especially spinal flexion), lasting 2-3 weeks followed by remissions and recurrences over months or even years before any leg pain appears; leg pain—more sharp and stabbing, running down back of thigh and lateral side of leg and foot.

Signs of Disc Protusion—A. Mechanical: flatness of the lumbar region, spasm of the erectores spinae, gross restriction of flexion of the spine, scoliosis to one or other side. B. Neurological: straight leg raising limited to 45° or less, wasting of the affected calf but no weakness, hypesthesia in area corresponding to distal distribution of L. 5 or S. I in the foot. C. Laboratory: Queckenstead test and protein level below involved disc were not found to be of value.

Suggested Mechanisms—(i) Low back pain due to ligamentous damage and muscle spasm; (ii) Pain in leg and foot real root pressure pain; (iii) Limited spinal flexion and Lasegue's sign and the flat lumbar region all guard against further stretching of the nerve; (iv) Variable scoliosis because the nerve root moves either way off the summit of the protusion.

Treatment. A. Medical Treatment—The essential feature was bed rest and it did not make appreciable difference whether patients were allowed to move about in bed or not. Analgesics, and heat to the back and thigh were used until symptoms start to abate, then graduated exercises were begun. The average stay in hospital was two months.

B. Surgical Treatment—Surgery should be reserved for those patients in whom prolonged rest has failed to give relief, or in whom immediate recurrence takes place after medical treatment has ended, or in whom return to work is desired at once for economic reasons, or where a patient must return to heavy manual labour.

J. H. M.

GYNAECOLOGY I

ABORTIONS—A STUDY WITH EMPHASIS ON TREATMENT. Capt. P. Peterson: Am. Jour. Obs. and Gyn., Vol, 54, August, 1947.

This article contains the results of a study of 7,042 pregnancies of which 15.35% ended in spontaneous abortion over a ten year period ending in 1946.

Successful pregnancies resulted from the treatment to be outlined in 64% of the habitual aborters as compared with only 27% in those untreated. Success occurred in 98.6% of non-habitual aborters.

Causes: Omitting defects of the fertilized ova causes were listed as infantile uterus, retrodisplacement of the uterus, low prothombin levels, low estrogenic effect, low gonadotropic effect, low progesterone effect and estrogen-progesterone effect.

Diagnosis: Following an abortion each patient was given a thorough study, including a good history, physical examination, B.M.R., glucose tolerance tests, Rh factor studies, prothombin level determination, endometrial biopsy, vaginal smears.

Treatment: Treatment was divided into (*a*) preconceptional, (*b*) postconceptional, (*c*) threatened abortion. The emphasis was placed on the pre- and postconceptional treatment as threatened abortion was little influenced by any treatment given other than bed rest.

In most cases preconceptional treatment was carried out for three months before pregnancy was attempted. Infantile uterus was treated by diethylstilbestrol and progesterone therapy. Retrodisplacement was corrected with a Findley pessary after an interval of three months following the abortion. Low prothombin levels were elevated and maintained with synthetic Vitamin K preparations. Therapy was given for a week before the menstrual period or expected date during pregnancy. Low estrogen effect was corrected by the use of stil-

bestrol exclusively, increasing the doses during pregnancy. This medication must be discontinued two months before term or postmaturity will be produced. Low gonadotropic effect was improved by the use of chorionic gonadotropic hormone, stilbestrol and progesterone. Low progesterone was least successfully improved with large doses of progesterone and chorionic gonadotropic hormone. Low oestrogen-progesterone effect was treated with stilbestrol and progesterone in large doses. For exact details the reader is referred to Dr. Peterson's article.

By the method outlined, substantial improvement was noted in the course of pregnancy in habitual aborters as well as non-habitual aborters.

J. S. L.

For Delicate Babies and Children...

You Can Safely Recommend

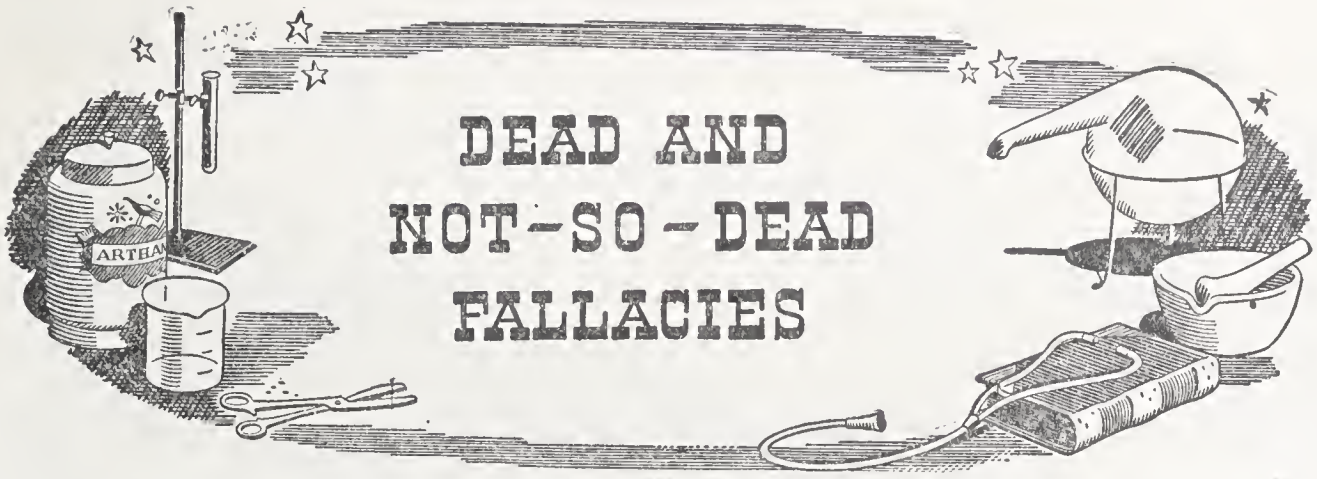
"FARMER'S WIFE"

PARTLY SKIMMED MILK

. . . promotes good bones and teeth . . . has higher protein value and lower fat content. Babies find it easier to digest. An excellent dietary source of Vitamin D-400 International Units per reconverted quart.

COW & GATE (CANADA) LIMITED
GANANOQUE, ONTARIO

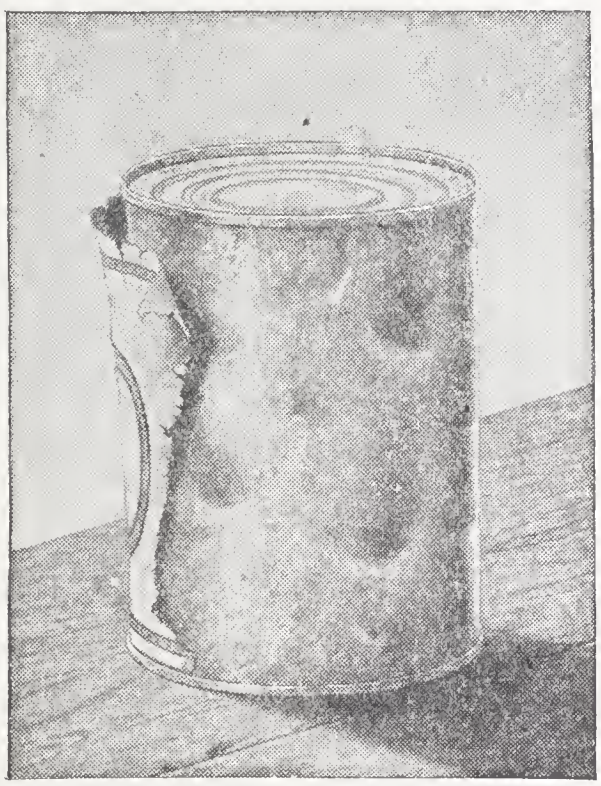
Please send for literature and pocket formula card.



DEAD AND NOT-SO-DEAD FALLACIES

In Siam years ago, after the birth of a first child, the mother alternately exposed her back and abdomen to a fire for 30 days.

It was believed that this torture appeased the gods and prevented the most direful consequences to both mother and child.



A great many people today believe that if there is rust on the outside of a can, the food inside is contaminated.

This is a fallacy. Unless the rust has pierced the metal, the contents of the can are perfectly safe and nutritious.

CANCO

AMERICAN CAN COMPANY

KENTVILLE • MONTREAL • HAMILTON • TORONTO • WINNIPEG • VANCOUVER

CANNED FOOD IS GRAND FOOD

A liver preparation with

an important new addition

AYERST LIVER EXTRACT with FOLIC ACID

No. 351

The excellent results obtained by the use of folic acid in pernicious and other macrocytic anaemias have suggested that the combined administration of folic acid and liver extract is more effective than either alone. Each dry powder capsule of Ayerst Liver Extract with Folic Acid contains the anti-pernicious anaemia principle obtained from 2/3 ounce of fresh liver in addition to 0.5 mg. of folic acid. Supplied in bottles of 100 capsules.

Other Ayerst Liver Extract Preparations

INJECTABLE • LIQUID • CAPSULES • POWDER

Ayerst

AYERST, McKENNA & HARRISON LIMITED
Biological and Pharmaceutical Chemists
MONTREAL CANADA

Old Way . . .

CURING RICKETS in the CLEFT of an ASH TREE

FOR many centuries,—and apparently down to the present time, even in this country—ricketic children have been passed through a cleft ash tree to cure them of their rickets, and thenceforth a sympathetic relationship was supposed to exist between them and the tree.

Frazer* states that the ordinary mode of effecting the cure is to split a young ash sapling longitudinally for a few feet and pass the child, naked, either three times or three times three through the fissure at sunrise. In the West of England, it is said the passage must be "against the sun." As soon as the ceremony is performed, the tree is bound tightly up and the fissure plastered over with mud or clay. The belief is that just as the cleft in the tree will be healed, so the child's body will be healed, but that if the rift in the tree remains open, the deformity in the child will remain, too, and if the tree were to die, the death of the child would surely follow.

*Frazer, J. G.: The Golden Bough, vol. 1, New York, Macmillan & Co., 1923

It is ironical that the practice of attempting to cure rickets by holding the child in the cleft of an ash tree was associated with the rising of the sun, the light of which we now know is in itself one of Nature's specifics.

New Way . . .

Preventing and Curing Rickets *with* MEAD'S OLEUM PERCOMORPHUM

NOWADAYS, the physician has at his command, Mead's Oleum Percomorphum, a Council-Accepted vitamin D product which actually prevents and cures rickets, when given in proper dosage.

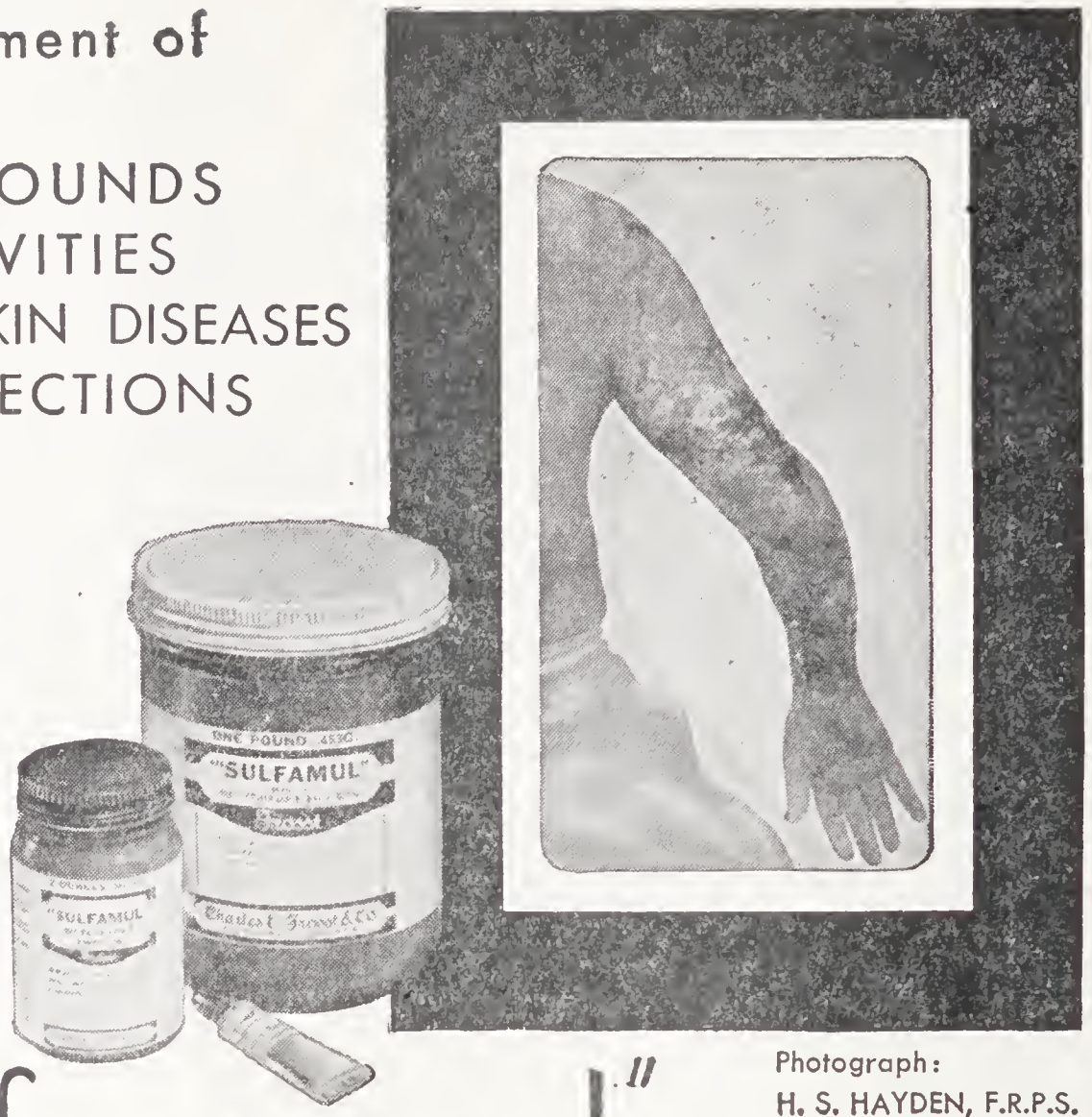
Like other specifics for other diseases, larger dosage may be required for extreme cases. It is safe to say that when used in the indicated dosage, Mead's Oleum Percomorphum is a specific in almost all cases of rickets, regardless of degree and duration.

Mead's Oleum Percomorphum because of its high vitamins A and D content is also useful in deficiency conditions such as tetany, osteomalacia and xerophthalmia.

COUNCIL-ACCEPTED: Oleum Percomorphum With Other Fish-Liver Oils and Viosterol. Contains 60,000 vitamin A units and 8,500 vitamin D units per gram and is supplied in 10 c.c. and 50 c.c. bottles; and in bottles containing 50 and 250 capsules.

MEAD JOHNSON & COMPANY OF CANADA, LTD., BELLEVILLE, ONTARIO

For the Treatment of
BURNS
INFECTED WOUNDS
ABSCESS CAVITIES
SUPERFICIAL SKIN DISEASES
VAGINAL INFECTIONS



Photograph:
H. S. HAYDEN, F.R.P.S.

"Sulfamul"

A non-adhesive, non-hydroscopic, stable emulsion containing
5% SULFATHIAZOLE "Frosst"

The most effective concentration . . . the most effective vehicle . . . the most effective method yet developed for local application of sulfathiazole. Sulfamul is applied with minimum discomfort to the patient, provides definite local anaesthetic action, requires no frequent changes of dressing, tends to shorten healing time, and promotes most satisfactory cosmetic results.

- *In the treatment of:*
  Infected Wounds, Abscess Cavities, Burns, Chronic Ulcers and Superficial Infections.
- *As a dressing for:*
  Burns about the face, hands and points of flexion.
- *As a non-adhesive bacteriostatic pack:*
  In the Vagina before and after operative procedures on the birth canal.
- *As a bacteriostatic packing in:*
  Infections about the cervix and vagina.

ADMINISTRATION

Sterile gauze is impregnated with Sulfamul and then packed with moderate firmness into abscess or other infected cavity. The pack may be left in position for periods up to 72 hours, surface changes only being made.

In superficial infections Sulfamul or Sulfamul impregnated gauze, may be directly applied.

MODES OF ISSUE: 2 oz., 1 lb. and 7½ lb. glass jars.

"SULFAMUL" OPHTHALMIC

(Sulfathiazole Emulsion 5% "Frosst")

For the treatment of eye infections such as Conjunctivitis and other pyogenic infections about the eyelids. Remarkable effects have been obtained where the emulsion has been applied locally.

Available in 1/8 oz. long nozzled, collapsible tubes.

Charles E. Frosst & Co.
MONTREAL CANADA

Frosst
SINCE 1899
THE SYMBOL OF PROGRESS
IN PHARMACEUTICAL RESEARCH

SYMBOLS OF SIGNIFICANCE

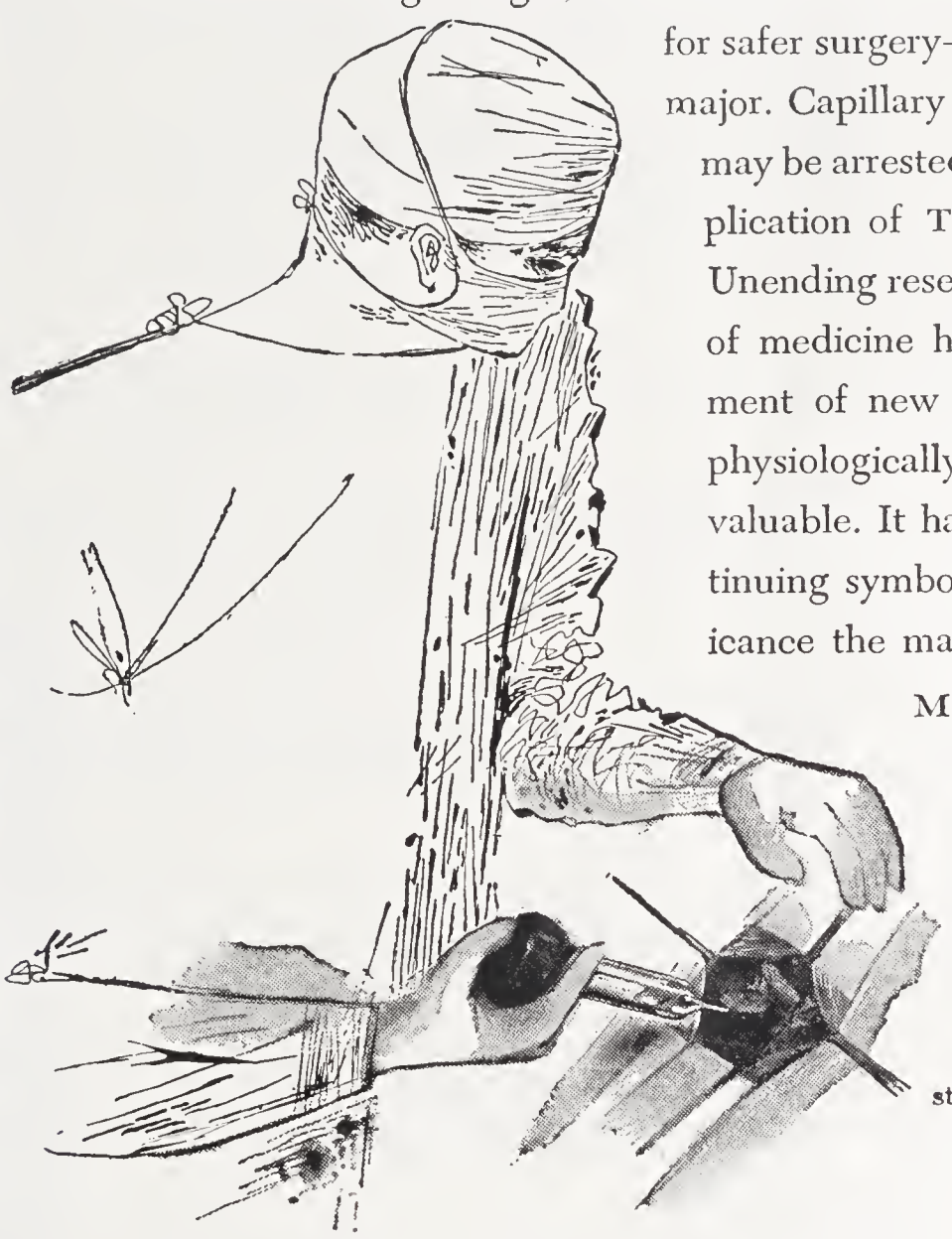
Thrombin Topical

(Bovine Origin)

"Hemostat, please... Thrombin."

Bleeding controlled, the operation proceeds. THROMBIN TOPICAL, highly potent, rapidly acting hemostatic of biologic origin, is a distinct achievement for safer surgery—minor and major. Capillary hemorrhage may be arrested seconds after local application of THROMBIN TOPICAL. Unending research in all the branches of medicine has led to the development of new Parke-Davis products, physiologically sound and clinically valuable. It has maintained as a continuing symbol of therapeutic significance the mark of Parke-Davis—

MEDICAMENTA VERA.



THROMBIN TOPICAL is available in 5,000-unit ampoules, each packed with a 5 cc. ampoule of sterile, isotonic saline diluent.

PARKE, DAVIS & COMPANY, LTD., WALKERVILLE, ONT.

MEDICAMENTA VERA · PD CO.

Facts regarding *fluidity*

of PENICILLIN in oil and wax

When penicillin in oil and wax is to be used once daily, the most important consideration is the maintenance of therapeutic blood levels for 24 hours.

For easy administration and adequately sustained blood levels, the formula must be neither too viscous nor too fluid . . . the penicillin crystals of correct size, shape and density . . . the container appropriate to the use intended. The following should also be recognized:

1 For administration from multiple-dose vials, the mixture should be sufficiently fluid to permit easy withdrawal, accurate measurement and easy injection.

2 In all fluid preparations, however, the penicillin has a tendency to settle out. Unless the container has adequate air space and volume to permit resuspension of the settled penicillin by shaking, 24 hour blood levels may not be maintained. Either overdosage or underdosage may result.

3 When injected from individual-dose cartridges, the penicillin in oil and wax suspension should be of slightly thicker consistency. If it is not, and the penicillin settles out, it cannot be resuspended by shaking, because (a) the volume is too small, and (b) the cartridge has no air space.

4 The slightly heavier type of suspension can be easily injected in accurate dosage with a minimum of discomfort to the patient. It is essentially free-flowing at room temperature, and each cartridge contains a full 1 cc. (300,000 unit) dose, which eliminates the need of measuring.

In keeping with Squibb policy of making the form of the product appropriate to the use, two forms of Squibb Penicillin G in Oil and Wax are available. Each offers the advantages of proper formula and consistency.

For easy, individual injections in home, office and emergency:

SQUIBB PENICILLIN G IN OIL AND WAX

Essentially free-flowing at room temperature: in Double-cell Cartridges for use with B-D* disposable or permanent syringe.

*T.M. REG. BECTON, DICKINSON & CO.

For easy, mass injections in clinic, hospital, or office, the new 10 cc. vial of

SQUIBB LIQUID PENICILLIN G IN OIL AND WAX

Resuspension readily attained; easy to inject; no withdrawal difficulties.

For Literature write

E. R. SQUIBB & SONS CANADA LIMITED

36-48 CALEDONIA ROAD • TORONTO

25-7A